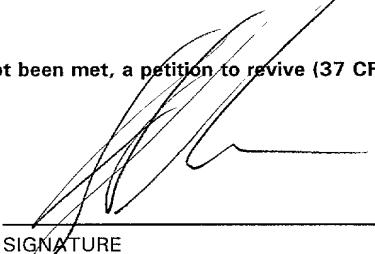
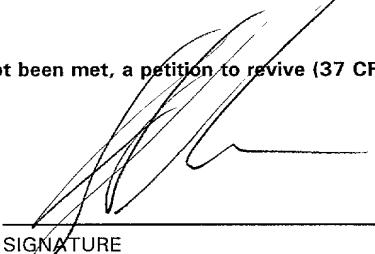


102010-1011 10AUG98

FORM-PTO-1390 (Rev. 10-96)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				012627-007
INTERNATIONAL APPLICATION NO. PCT/DE97/00245		INTERNATIONAL FILING DATE 10 February 1997		PRIORITY DATE CLAIMED 9 February 1996
TITLE OF INVENTION SPERMATOGENESIS CONTROL				
APPLICANT(S) FOR DO/EO/US Gunther SCHÜTZ, Julie A. BLENDY, Klaus KÄSTNER, Gerhard WEINBAUER, Eberhard NIESCHLAG				
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:				
<p>1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and the PCT Articles 22 and 39(1).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</p> <p>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ul style="list-style-type: none"> a. <input checked="" type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US) </p> <p>6. <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ul style="list-style-type: none"> a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> have been transmitted by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. </p> <p>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input checked="" type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p>				
Items 11. to 16. below concern other document(s) or information included:				
<p>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A FIRST preliminary amendment.</p> <p><input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</p> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input type="checkbox"/> Other items or information:</p>				

U.S. APPLICATION NO. (if known) see 37 CFR 1.80 09/117810		INTERNATIONAL APPLICATION NO. PCT/DE97/00245	ATTORNEY'S DOCKET NUMBER 012627-007
17. <input checked="" type="checkbox"/> The following fees are submitted:		CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)): Search Report has been prepared by the EPO or JPO \$930 International preliminary examination fee paid to USPTO (37 CFR 1.482) \$720.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) \$790.00 Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$1070.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) \$98.00			
ENTER APPROPRIATE BASIC FEE AMOUNT =		\$ 930	
Surcharge of \$130.00 for furnishing the oath or declaration later than months from the earliest claimed priority date (37 CFR 1.492(e)). <input type="checkbox"/> 20 <input type="checkbox"/> 30		\$	
Claims	Number Filed	Number Extra	Rate
Total Claims	4 -20 =	0	X\$22.00
Independent Claims	-3 =		X\$82.00
Multiple dependent claim(s) (if applicable)		+ \$270.00	
TOTAL OF ABOVE CALCULATIONS =		\$ 930	
Reduction for 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).		\$	
SUBTOTAL =		\$ 465	
Processing fee of \$130.00 for furnishing the English translation later than months from the earliest claimed priority date (37 CFR 1.492(f)). <input type="checkbox"/> 20 <input type="checkbox"/> 30		+	\$
TOTAL NATIONAL FEE =		\$ 465	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property +		\$	
TOTAL FEES ENCLOSED =		\$ 465	
<input type="checkbox"/> Amount to be: refunded \$ <input type="checkbox"/> charged \$ 			
a. <input checked="" type="checkbox"/> A check in the amount of \$ <u>465.00</u> to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. <u>02-4800</u> in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>02-4800</u> . A duplicate copy of this sheet is enclosed.			
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.			
SEND ALL CORRESPONDENCE TO: Teresa Stanek Rea BURNS, DOANE, SWECKER & MATHIS, L.L.P. P.O. Box 1404 Alexandria, Virginia 22313-1404			
 SIGNATURE <u>Teresa Stanek Rea</u> NAME <u>30,427</u> REGISTRATION NUMBER			

Applicant or Patentee: Gunther SCHUTZ et al
Application or Patent No.: 09/117,810
Filed or Issued: _____
For: SPERMATOGENESIS CONTROL

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 C.F.R. §§ 1.9(f) AND 1.27(d)) - NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION DEUTSCHES KREBSFORSCHUNGSZENTRUM
STIFTUNG DES ÖFFENTLICHEN RECHTS

ADDRESS OF ORGANIZATION Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany

TYPE OF ORGANIZATION

- University or other institution of higher education
 Tax exempt under Internal Revenue Service Code (26 U.S.C. §§ 501(a) and 501(c)(3))
 Nonprofit scientific or educational under statute of state of The United States of America
(Name of state _____)
(Citation of statute _____)
 Would qualify as tax exempt under Internal Revenue Service Code (26 U.S.C. §§ 501(a) and 501(c)(3)) if located in The United States of America
 Would qualify as nonprofit scientific or educational under statute of The United States of America if located in The United States of America
(Name of state _____)
(Citation of statute _____)

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 C.F.R. § 1.9(e) for purposes of paying reduced fees under Sections 41(a) and 41(b) of Title 35, United States Code, with regard to the invention entitled by inventor(s) Gunther SCHUTZ; Julie BLENDY; Klaus KASTNER; Gerhard WEINBAUER; Eberhard NIESCHLAG described in

- the specification filed herewith
 Application No. 09/117,810, filed _____
 Patent No. _____, issued _____

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above-identified invention.

If the rights held by the above-identified nonprofit organization are not exclusive, each individual, concern, or organization having rights to the invention is listed below,* and no rights to the invention are held by any person, other than the inventor, who would not qualify as an individual inventor under 37 C.F.R. § 1.9(c), or by any concern that would not qualify as either a small business concern under 37 C.F.R. § 1.9(d) or a nonprofit organization under 37 C.F.R. § 1.9(e).

000100730 000000000000

Application No. 09/117,810
Attorney's Docket No. 012627-007

*NOTE: Separate verified statements are required from each named person, concern, or organization having rights to the invention averring to their status as small entities. (37 C.F.R. § 1.27.)

FULL NAME _____

ADDRESS _____

individual small business concern nonprofit organization

FULL NAME _____

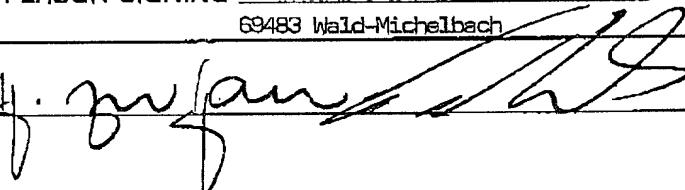
ADDRESS _____

individual small business concern nonprofit organization

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earlier of the issue fee and any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 C.F.R. § 1.28(b).)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Prof.Dr.med.Dr.h.c.mult.H.zur Hausen Dr.iner.pol. J. Puchta
TITLE IN ORGANIZATION Chairman a. Scient.Member of the Board Adm.Member of the Board
ADDRESS OF PERSON SIGNING Eichenstraße 1 Eichenweg 1
69483 Wald-Michelbach 69198 Schriesheim

SIGNATURE 

DATE September 28, 1998

09/117810

201 Rec'd PCT/PTO 10 AUG 1998

Attorney's Docket No. 012627-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
Günther Schütz et al) Group Art Unit: Unassigned
Application No.: Unassigned) Examiner: Unassigned
(Corresponds to PCT/DE97/00245))
International Filing)
Date: 10 February 1997)
For: SPERMATOGENESIS CONTROL)

PRELIMINARY AMENDMENT

BOX PCT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination on the merits, please amend the
above-captioned application as follows:

IN THE CLAIMS:

Kindly amend the claims as follows:

Claim 3, line 2, delete "or 2".

REMARKS

Entry of the foregoing amendment is respectfully
requested.

The claims have been amended to eliminate multiple
dependency and to place them in better condition for U.S.
patent practice.

Should the Examiner have any questions concerning the
subject application, a telephone call to the undersigned would
be appreciated.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____

Teresa Stanek Rea
Registration No. 30,427

Post Office Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: August 10, 1998

Spermatogenesis Control

The present invention relates to a pharmaceutical composition for spermatogenesis control and a process for investigating the spermatogenesis as well as a kit usable therefor.

The development of spermia is referred to as spermatogenesis. It is desired to interfere in spermatogenesis if the latter is unbalanced and does not yield functioning spermia. On the other hand, interference in spermatogenesis could also be made use of to carry out a fertility control in male persons.

Therefore, it is the object of the present invention to provide a product by which spermatogenesis can be controlled.

According to the present invention this is achieved by the subject matters defined in the claims.

Therefore, the subject matter of the present invention relates to a pharmaceutical composition adapted to control spermatogenesis. Such a composition comprises:

- (a) for positive control
 - one or more substances of
 - CREM (cAMP responsive element modulator), a CREM-phosphorylating compound and a CREM expression inducing compound, and/or

- (b) for negative control
 - one or more substances of
 - a CREM-inhibiting compound, a CREM phosphorylation inhibiting compound, and a CREM expression inhibiting compound.

The present invention is based on the applicant's finding that CREM (cAMP responsive element modulator) is a decisive regulator of spermatogenesis. The applicant has found that CREM is a transcription factor which controls the expression of proteins involved in spermatogenesis. These proteins are referred to as CREM-dependent proteins in the present application. Examples thereof are proacrosin, protamine, Tp-1 (transition protein-1), MCS (mitochondrial capsule seleno protein) and RT7 (mill germ cell specific protein). If there is CREM deficiency, i.e. if CREM is not expressed or expressed only to a reduced extent and not expressed in phosphorylated form, respectively, so that the above proteins are not expressed either or expressed only to a reduced extent, there will be unbalanced spermatogenesis which results in non-functioning spermia.

In a pharmaceutical composition of the present invention, the expression "a CREM-phosphorylated compound" refers to any compounds adapted to phosphorylate CREM, particularly kinases. In addition, the expression "a CREM expression inducing compound" relates to any compounds which can directly or indirectly induce the expression of CREM. Moreover, the expression "a CREM-inhibiting compound" covers any compounds adapted to inhibit CREM, particularly antibodies directed against CREM. Besides, the expression "a CREM phosphorylation inhibiting compound" denotes any compounds adapted to inhibit the phosphorylation of CREM. Such compounds are particularly kinase-inhibitors, such as H7, H8, H89, HA 1004 and Walsh inhibitor. Furthermore, the expression "a CREM expression inhibiting compound" comprises any compounds which can directly or indirectly inhibit the expression of CREM.

The person skilled in the art knows how to determine which substances mentioned for a pharmaceutical composition of the present invention and which amounts thereof are the best for the spermatogenesis control in an individual proband. For example, the following offers itself to the person skilled in the art: preparation of a transgenic mouse which

which expresses an inducible CREB (cyclic AMP responsive element binding protein) mutant, in round spermatids of the testis. This mutant dimerizes with CREM, the mutant being dominant-negative over CREM, i.e. CREM is inhibited by dimerization with dominant-negative CREB. Therefore, the transgenic mouse enables the determination of substances and the amounts thereof, which influence CREM and thus spermatogenesis.

The introduction of a vector containing a promoter enabling the gene expression in round spermatids, such as the protamine promoter (cf. Zambrowicz, B.P. et al., Proc. Natl. Acad. Sci., U.S.A. 90, (1990), 5071-5075) into inseminated oocytes of a mouse, offers itself for the preparation of the transgenic mouse. This promoter controls a DNA which codes for a fusion protein from the mutated CREB and a modified ligand binding domain of the human progesterone receptor (cf. Wang, Y. et al., Proc. Natl. Acad. Sci., U.S.A. 91, (1994), 8180-8184). The mutated CREB does not have serine but alanine at position 133 and thus cannot be phosphorylated, which signifies the loss of its transcription activity. Amino acids 892-933 are lacking in the modified ligand binding domain of the human progesterone receptor, so that this ligand binding domain can no longer be bound by progesterone but only by the ligand RU 486. The latter serves for activating the mutated CREB in the fusion protein.

A process is also provided according to the invention, which is suited to investigate spermatogenesis and control it, respectively. Such a process comprises the determination of CREM and/or CREM-dependent proteins, e.g. proacrosin, protamine, Tp-1, MCS and RT7.

It is possible to use common methods for determining CREM and/or CREM-dependent proteins. It is favorable to determine by means of PCR methods whether the DNA sequences coding for CREM and/or CREM-dependent proteins include mutations. In addition, the possibility presents itself to puncture the

testis to investigate preferably spermatids and more preferably round spermatids of testes and determine the expression of CREM and/or CREM-dependent proteins. For this purpose, CREM and/or CREM-dependent proteins can be determined in a Western blot analysis in which antibodies are used against the individual proteins. The mRNA of CREM and/or CREM-dependent proteins can also be determined in a Northern blot analysis in which DNAs of the individual proteins are used as samples.

A kit is also provided according to the invention, which is suited to determine CREM and/or CREM-dependent proteins. Such a kit comprises:

One or more of (a) to (c)

- (a) primers for amplifying DNA coding for CREM and/or CREM-dependent proteins,
- (b) antibodies against CREM and/or CREM-dependent proteins, e.g. proacrosin, protamine, Tp-1, MCS and RT7,
- (c) DNA samples for mRNA of CREM and/or CREM-dependent proteins, e.g. proacrosin, protamine, Tp-1, MCS and RT7, as well as
- (d) standards and detection reagents for one or more of (a) to (c), and
- (e) carriers as well as conventional vehicles.

By means of the present invention it is possible to control spermatogenesis, i.e. positively control an unbalanced spermatogenesis, so as to produce functioning spermia and to negatively control normal spermatogenesis thereby inhibiting the formation of spermia. The control of spermatogenesis is reversible, so that the negative control is particularly suitable to control the fertility of a male animal, particularly a male person. By means of the present

invention it is also possible to monitor spermatogenesis, which will be of special importance if controlling interference has been made.

Amended Claims

1. A process for investigating spermatogenesis and monitoring it, respectively, wherein CREM and/or CREM-dependent proteins are determined.
2. The process according to claim 1, characterized in that the CREM-dependent proteins are proacrosin, protamine, Tp-1, MCS and/or RT7.
3. A kit for carrying out the process according to claim 1 or 2, comprising one or more of (a) to (e)
 - (a) primers for amplifying DNA coding for CREM and/or CREM-dependent proteins,
 - (b) antibodies against CREM and/or CREM-dependent proteins,
 - (c) DNA samples for mRNA of CREM and/or CREM-dependent proteins, as well as
 - (d) standards and detection reagents for one or more of (a) to (c), and
 - (e) carriers as well as conventional vehicles.
4. A kit according to claim 5, characterized in that the CREM-dependent proteins are proacrosin, protamine, Tp-1, MCS and/or RT7.

Abstract of the Disclosure

The present invention relates to a pharmaceutical composition, comprising

- (a) for positive control
 - one or more substances of
 - CREM, a CREM-phosphorylating compound and a CREM expression inducing compound, and/or
 - (b) for negative control
 - one or more substances of
 - a CREM-inhibiting compound, a CREM phosphorylation inhibiting compound, and a CREM expression inhibiting compound.

In addition, the invention concerns a process for investigating spermatogenesis as well as a kit usable for therefor.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to Provisional and PCT International Applications)ATTORNEY'S DOCKET NUMBER
012627-007

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

SPERMATOGENESIS CONTROL

the specification of which (check only one item below):

- is attached hereto.
 was filed as United States application

Number _____
on _____
and was amended
on _____ (if applicable).

- was filed as PCT international application

Number PCT/DE97/00245
on 10 February 1997
and was amended under PCT Article 19
on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(e) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. §119:

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 U.S.C. §119
DE	196 04 773.0	09 February 1996	<u>X</u> Yes <u> </u> No
			<u> </u> Yes <u> </u> No
			<u> </u> Yes <u> </u> No
			<u> </u> Yes <u> </u> No
			<u> </u> Yes <u> </u> No

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONTINUED)
(Includes Reference to Provisional and PCT International Applications)

ATTORNEY'S DOCKET NO.
012627-007

I hereby claim the benefit under Title 35, United States Code, §120 of any United States applications(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the Office all information known to me to be material to the patentability as defined in Title 37, Code of Federal Regulations §1.56, which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS (check one)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

PCT APPLICATIONS DESIGNATING THE U.S.		
PCT APPLICATION NO.	PCT FILING DATE	U.S. APPLICATION NUMBERS ASSIGNED (if any)

I hereby appoint the following attorneys and agent(s) to prosecute said application and to transact all business in the Patent and Trademark Office connected therewith and to file, prosecute and to transact all business in connection with international applications directed to said invention:

William L. Mathis	<u>17,337</u>	George A. Hovanec, Jr.	<u>28,223</u>	Peter K. Skiff	<u>31,917</u>
Peter H. Smolka	<u>15,913</u>	James A. LaBarre	<u>28,632</u>	Richard J. McGrath	<u>29,195</u>
Robert S. Swecker	<u>19,885</u>	E. Joseph Gess	<u>28,510</u>	Matthew L. Schneider	<u>32,814</u>
Platon N. Mandros	<u>22,124</u>	R. Danny Huntington	<u>27,903</u>	Michael G. Savage	<u>32,596</u>
Benton S. Duffett, Jr.	<u>22,030</u>	Eric H. Weisblatt	<u>30,505</u>	Gerald F. Swiss	<u>30,113</u>
Norman H. Stepno	<u>22,716</u>	James W. Peterson	<u>26,057</u>	Michael J. Ure	<u>33,089</u>
Ronald L. Grudziecki	<u>24,970</u>	Teresa Stanek Rea	<u>30,427</u>	Charles F. Wieland III	<u>33,096</u>
Frederick G. Michaud, Jr.	<u>26,003</u>	Robert E. Krebs	<u>25,885</u>	Bruce T. Wieder	<u>33,815</u>
Alan E. Kopecki	<u>25,813</u>	William C. Rowland	<u>30,888</u>	Todd R. Walters	<u>34,040</u>
Regis E. Slutter	<u>26,999</u>	T. Gene Dillahunty	<u>25,423</u>		
Samuel C. Miller, III	<u>27,360</u>	Patrick C. Keane	<u>32,858</u>		
Ralph L. Freeland, Jr.	<u>16,110</u>	Bruce J. Boggs, Jr.	<u>32,344</u>		
Robert G. Mukai	<u>28,531</u>	William H. Benz	<u>25,952</u>		

and:

Address all correspondence to:

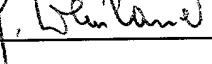
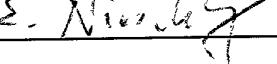
Teresa Stanek Rea
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, Virginia 22313-1404

Address all telephone calls to: Teresa Stanek Rea

at (703) 836-6620.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONTINUED)
(Includes Reference to Provisional and PCT International Applications)ATTORNEY'S DOCKET NO.
012627-007

FULL NAME OF SOLE OR FIRST INVENTOR <u>Günther SCHÜTZ</u>	SIGNATURE 	DATE 27/11/98
RESIDENCE Zeppelinstrasse 86, D-69121 Heidelberg, Germany	DEX	CITIZENSHIP DE
POST OFFICE ADDRESS Zeppelinstrasse 86, D-69121 Heidelberg, Germany		
FULL NAME OF SECOND JOINT INVENTOR, IF ANY <u>Julie A. RLENDY</u>	SIGNATURE 	DATE 21/11/99
RESIDENCE Kastanienweg 8, D-69221 Dossenheim, Germany	PH 622 UNIVERSITY PL. SWARTHMORE, PA 19081 X K.U. GB	CITIZENSHIP DE U.S. X GB
POST OFFICE ADDRESS Kastanienweg 8, D-69221 Dossenheim, Germany	622 UNIVERSITY PL. SWARTHMORE, PA 19081 X GB	
FULL NAME OF THIRD JOINT INVENTOR, IF ANY <u>Klaus KÄSTNER</u> X K.U.	SIGNATURE 	DATE 12/11/98
RESIDENCE Kastanienweg 8, D-69221 Dossenheim, Germany	PH 622 UNIVERSITY PL. SWARTHMORE, PA 19081 K.U.	CITIZENSHIP DE
POST OFFICE ADDRESS Kastanienweg 8, D-69221 Dossenheim, Germany	622 UNIVERSITY PL. SWARTHMORE, PA 19081 X K.U.	
FULL NAME OF FOURTH JOINT INVENTOR, IF ANY <u>Gerhard WEINBAUER</u>	SIGNATURE 	DATE 22/3/99
RESIDENCE Idenbrockplatz 16, D-68159 Munster, Germany	DEX	CITIZENSHIP DE
POST OFFICE ADDRESS Idenbrockplatz 16, D-68159 Munster, Germany		
FULL NAME OF FIFTH JOINT INVENTOR, IF ANY <u>Eberhard NIESCHLAG</u>	SIGNATURE 	DATE 3/12/99
RESIDENCE Gremmendorfer Weg 91, D-48167 Munster, Germany	DEX	CITIZENSHIP DE
POST OFFICE ADDRESS Gremmendorfer Weg 91, D-48167 Munster, Germany		
FULL NAME OF SIXTH JOINT INVENTOR, IF ANY	SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		
FULL NAME OF SEVENTH JOINT INVENTOR, IF ANY	SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		
FULL NAME OF EIGHTH JOINT INVENTOR, IF ANY	SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		
FULL NAME OF NINTH JOINT INVENTOR, IF ANY	SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		